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Ranitidine Oral Solution

» Ranitidine Oral Solution is a solution of Ranitidine Hydrochloride in water. It contains the equivalent of not less than 90.0 percent and not more than 110.0 percent of the labeled amount of ranitidine ($C_{13}H_{22}N_4O_3S$).

Packaging and storage—Preserve in tight, light-resistant containers. Store below 25°. Do not freeze.

USP Reference standards ⟨11⟩—

USP Ranitidine Hydrochloride RS

USP Ranitidine Related Compound A RS

5-[[(2-Aminoethyl)thio]methyl]-*N*,*N*-dimethyl-2-furanmethanamine, hemifumarate salt.

USP Ranitidine Related Compound C RS

N-{2-[({5-[(Dimethylamino)methyl]-2-furanyl}methyl)sulfinyl]ethyl}-*N*'-methyl-2-nitro-1,1-ethenediamine.

Identification—

A: The R_F value of the principal spot observed in the chromatogram of the *Test preparation* obtained as directed in the *Chromatographic purity* test corresponds to that obtained from the *Standard preparation.*

B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay.*

Microbial enumeration tests ⟨61⟩ and Tests for specified microorganisms ⟨62⟩—It meets the requirements of the tests for absence of *Salmonella* species and *Escherichia coli;* and the total aerobic microbial count does not exceed 100 cfu per mL.

pH ⟨791⟩: between 6.7 and 7.5.

Chromatographic purity—

Test preparation—[Note—Apply a quantity of extractives from Oral Solution to the chromatographic plate so as to achieve a nominal loading of 200 µg of ranitidine.] Transfer a weighed quantity of Oral Solution, equivalent to 10 mg of ranitidine, to a suitable syringe. Attach the tip of the syringe to the top of a cartridge (11 mm × 12 mm) of volume 0.5 mL containing 0.4 g of an L1 packing for high-pressure liquid chromatography that has been previously prepared by passage of 10 mL of methanol followed by passage of 20 mL of 0.5 M ammonia solution. Add 2.0 mL of 0.5 M ammonia solution to the syringe and force the mixture slowly through the cartridge. Repeat with 2 further 3-mL portions of 0.5 M ammonia solution. Discard all the liquid that has traversed the cartridge. Pass 5 mL of a mixture of 0.1 M hydrochloric acid and methanol (3:1) through the cartridge, and collect the eluant in a clean round-bottom, 25-mL flask. Repeat this with another 5-mL portion of the same eluting mixture and collect the eluant in the same flask. Evaporate the contents of the flask to dryness at a temperature not exceeding 30°. Redissolve the residue in 1.0 mL of a mixture of methanol and water (50:50).

Standard preparation—Dissolve USP Ranitidine Hydrochloride RS in a mixture of methanol and water (50:50) to obtain a solution having a known concentration of 448 µg (equivalent to 400 µg of ranitidine) per mL. Dilute portions of this *Standard preparation* quantitatively with the mixture of methanol and water (50:50) to obtain solutions having concentrations of 224 µg per mL *(Diluted standard preparation A),* 112 µg per mL *(Diluted standard preparation B),* 56 µg per mL *(Diluted standard preparation C),* 22 µg per mL *(Diluted standard preparation D),* and 11 µg per mL *(Diluted standard preparation E),* respectively.

Resolution preparation—Dissolve USP Ranitidine Related Compound A RS in methanol to obtain a solution having a known concentration of 1.27 mg per mL.

Procedure—Apply separately 10 µL of the *Standard preparation,* the *Diluted standard preparations (A, B, C, D,* and *E),* and 20 µL (superposition of 2 × 10 µL) of the *Test preparation* to a suitable thin-layer chromatographic plate (see *Chromatography ⟨621⟩*) coated with a 0.25-mm layer of chromatographic silica gel mixture. In addition, apply separately a further loading of 10 µL of the *Test preparation* to the same plate, and on top of this application, apply 10 µL of the *Resolution preparation.* Allow the spots to dry, and develop the chromatograms in a solvent system consisting of a mixture of ethyl acetate, isopropyl alcohol, ammonium hydroxide, and water (25:15:5:1) until the solvent front has moved not less than 15 cm from the origin. Remove the plate from the developing chamber, mark the solvent front, and allow to air-dry. Expose the plate to iodine vapors in a closed chamber until the chromatogram is fully revealed. Examine the plate and compare the intensities of any secondary spots observed in the chromatogram of the *Test preparation* with those of the principal spots in the chromatograms of the *Standard preparation* and *Diluted standard preparations (A, B, C, D,* and *E):* the system suitability requirements are met when there is complete resolution between the primary spots of the *Test preparation* and the *Resolution preparation* and if a spot is observed in the chro matogram of

Diluted standard preparation E. The major secondary spot is not greater in size or intensity than the principal spot produced by the *Standard preparation* (2.0%), and no other secondary spot is greater in size or intensity than the principal spot produced by *Diluted standard preparation A* (1.0%). The sum of the intensities of all secondary spots obtained from the *Test preparation* corresponds to not more than 5.0%. [NOTE—Spots established as arising from other components in the formulation are to be ignored.]

Assay—

Mobile phase, Standard preparation, System suitability solution, and *Chromatographic system*—Prepare as directed in the *Assay* under *Ranitidine Injection*, the chromatographic column being fitted with a suitable pre-column also containing packing L1.

Assay preparation—Dilute an accurately measured quantity of Oral Solution, quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution having a concentration of 0.1 mg of ranitidine per mL.

Procedure—Separately inject an equal quantity (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the area responses for the major peaks. Calculate the quantity, in mg, of ranitidine ($C_{13}H_{22}N_4O_3S$) in the portion of Oral Solution taken by the formula:

$$(314.40/350.87)(L/D)(C)(r_U/r_S)$$

in which 314.40 and 350.87 are the molecular weights of ranitidine and ranitidine hydrochloride respectively; L is the labeled quantity of ranitidine in the Oral Solution taken; D is the concentration, in mg per mL, of ranitidine in the *Assay preparation*, on the basis of the labeled quantity and the extent of dilution; C is the concentration, in mg per mL, of USP Ranitidine Hydrochloride RS in the *Standard preparation;* and r_U and r_S are the peak area responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
RANITIDINE ORAL SOLUTION	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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